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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS - REGISTRATION DIVISION (7505P)

DP BARCODE No.: 400991, 399312, 395006; EPA Reg. No.: 88685-R; DECISION No.: 455232
PRODUCT NAME: Glufosinate-Ammonium Technical; PC Code(s): 128850; ACTION CODE: R310

DATE: April 17, 2012

SUBJECT: Product Chemistry Review of Glufosinate-Ammonium Technical TGA1

FROM: Akiva Abramovitch, Ph.D.
Technical Review Branch / RD (7505P)

THROUGH: Shyam Mathur, Ph. D.
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Technical Review Branch/RD (7505P)

Shyam 4/19/12

TO: Michael Walsh / Kathryn Montague, RM 23
Herbicide Branch / RD (7505P)

DECISION No.: 455232
File Symbol No.: 88685-R
PRODUCT NAME: Glufosinate-Ammonium Technical
PC Code: 128850
REGISTRANT: Orion GFS, LLC
USE: Herbicide
FOOD USE: Yes ☒ No ☐
MRID Numbers: 486073-01 through 486073-03

INTRODUCTION:

The registrant submitted Group B data in MRID 487894-01 to address deficiencies cited in previous communications and supplement the previously submitted application for the registration of glufosinate-ammonium TGA1 produced by [REDACTED]

The registrant has previously submitted a proposed CSF for basic formulation dated 9-10-11 and the supporting group A data with MRIDs 486073-01 through 486073-03). The registrant has claimed that the proposed Glufosinate-Ammonium TGA1/MUP is substantially similar to the registered product Glufosinate-Ammonium Technical (manufactured by AgrEvo USA Co., N. Muskegon, MI), with Reg. No. 264-646.

TRB has been asked to evaluate the product chemistry data submitted and determine the acceptability of the data and CSF dated September 10, 2011.

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PRODUCT NAME: Glufosinate-Ammonium Technical; PC Code(s): 128850; ACTION CODE: R310;

SUMMARY OF FINDINGS:

1. Group A guidelines:

830.1550 (Product identity & composition)

Data for the identity and composition of the product were provided. The active ingredient is present at a nominal concentration of 98.6%. The nominal concentrations given on the CSF for the impurities present in the product at >0.1% w/w do not agree with the results of the preliminary analysis but an acceptable explanation was provided. The product chemistry data submitted corresponding to Guideline 830.1550 satisfy the data requirements of 40CFR§158.320.

830.1600 (Description of materials used to produce the product)

The registrant provided a list of suppliers and MSDSs for the materials used to produce the product. The product chemistry data submitted corresponding to Guideline 830.1600 satisfy the data requirements of 40CFR§158.325.

830.1620 (Description of production process)

A description of the production process at the [REDACTED] facility was provided. The product chemistry data submitted corresponding to Guideline 830.1620 satisfy the data requirements of 40CFR§158.330.

830.1670 (Discussion on the formation of impurities)

A discussion of the origin and mechanism formation for the impurities in the product was provided. The product chemistry data submitted corresponding to Guideline 830.1670 satisfy the data requirements of 40CFR§158.340.

830.1700 (Preliminary analysis)

Results of a five-batch preliminary analysis were provided, and the content of a.i. ranged from 98.6% to 100.2%. The product chemistry data submitted corresponding to Guideline 830.1700 satisfy the data requirements of 40CFR§158.345.

830.1750 (Certified limits)

Certified limits were provided for the active ingredient, and upper certified limits were provided for the impurities in the product. The proposed certified limits of the impurities in the CSF do not concur with the results of five batch analyses for the impurities but the registrant provided acceptable explanation how the proposed certified limits have been calculated in the CSF (dated 09-10-11). The data requirements was satisfied

830.1800 (Enforcement analytical method)

A description of the enforcement analytical method was provided. The active ingredient content was quantified using HPLC/UV. The method was validated for accuracy, precision, and linearity. The product chemistry data submitted corresponding to Guideline 830.1800 satisfy the data requirements of 40CFR§158.355.

830 series group B guidelines (physical-chemical properties)

The registrant submitted Group B data in MRID 487894-01 and satisfied data requirements with the exception of storage stability and corrosion data

Product ingredient source information may be entitled to confidential treatment

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CONCLUSIONS:

The TRB has reviewed the product chemistry data submitted for Glufosinate-Ammonium Technical (produced by [REDACTED]) and has concluded that the data requirements have been satisfied with the exception of the storage stability and corrosion data.:

1. The product chemistry data submitted for guideline 830 Series group A are acceptable.
2. The product chemistry data corresponding to 830 series group B (physical-chemical properties) are acceptable but storage stability and corrosion data remain as data gaps
3. The nominal concentrations given on the CSF for the impurities present in the product at >0.1% w/w do not agree with the results of the preliminary analysis but the registrant provided an acceptable explanation on how the certified limits for the impurities have been calculated.
4. This product with a label nominal concentration of 98.6% and the cited product EPA Reg. No. 264-646 are not substantially similar since the cited product is only 95% pure product and below the lower certified limits of this product.
5. The registrant addressed the issues related to the nominal concentrations of the active ingredients and the impurities. The lower certified limit of the active ingredient 95.6% is above the nominal concentration of the cited product.
6. The CSF dated September 10, 2011 is acceptable (The pH was corrected to 3.75 based on the Group B data-reported as 7 on the CSF in box 8).

830.1550. Product identity & composition: (MRID No. 486073-01)

Common Name: Glufosinate

Chemical name (CAS): Ammonium (±)-2-amino-4-(hydroxymethylphosphinyl)butanoate

(IUPAC): Ammonium 4-[hydroxyl(methyl)phosphinoyl]-DL-homoalaninate OR ammonium DL-homoalanin-4-yl(methyl)phosphinate

CAS No.: 77182-82-2

PC Code No.: 128850

Empirical Formula: C₅H₁₅N₂O₄P

Molecular Weight: 198.2

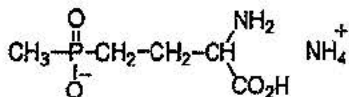


Table 1. Manufacturing and Impurity Data for Glufosinate-Ammonium Technical TGA1				
GLN	Requirement	MRID	Status	Details and /or Deficiency
830.1550	Product Identity and composition	486073-01	A	The nominal concentration of a.i. (98.6%) is supported by the five-batch analysis and agrees with the product label. The nominal concentrations given on the CSF for the impurities present in the product at >0.1% w/w do not agree with the results of the preliminary analysis, and no explanation was provided.
830.1600	Description of materials used to produce the product	486073-01	A	An acceptable description and composition of the starting materials was provided.
830.1620	Description of production process	486073-01	A	An acceptable description of the production process was provided.
830.1670	Discussion of formation of impurities	486073-01	A	The impurities potentially present in the product were identified and their origins were provided.
830.1700	Preliminary analysis	486073-02	A	Acceptable results of a five-batch analysis were provided.
830.1750	Certified limits	486073-01	A	The lower certified limit for the active ingredient is based on the standard lower certified limit. The upper certified limit is 100%. Upper certified limits were provided for the impurities present in the product at >0.1%. The registrant has proposed non- standard certified limits for the impurities, but no justifications have been given.
830.1800	Enforcement analytical method	486073-02 486073-03	A	The a.i. content is determined using HPLC/UV. The method was validated for accuracy, precision, and linearity.
A = Acceptable; N = Unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress ; U = Up-grade (additional information required);				

830 Series Subgroup B (Physical-Chemical Properties)

Table 2: Physical and Chemical Properties of Diflubenzuron Technical TGA1				
GLN	Requirement	MRID	Status	Result or Deficiency
830.6302	Color	487894-01	A	White
830.6303	Physical state	487894-01	A	Solid, powder
830.6304	Odor	487894-01	A	No odor
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	487894-01	A	Stable under conditions of manufacture and storage. Does not come into contact with metals/metal ions/high temperatures.
830.6314	Oxidation/reduction; chemical incompatibility	487894-01	A	Stable to oxidizing and reducing agents.
830.6315	Flammability		N/A	Solid product
830.6316	Explosibility		N/A	None
830.6317	Storage stability		I	Ongoing.
830.6319	Miscibility		N/A	Solid product
830.6320	Corrosion characteristics		I	Ongoing.
830.7000	pH	487894-01	A	3.75
830.7050	UV/Visible absorption		W	
830.7100	Viscosity		N/A	Solid product
830.7200	Melting point	487894-01	A	209 C (decompose)
830.7220	Boiling point		N/A	Solid product
830.7300	Density	487894-01	A	1.373 gm/ml
830.7370	Dissociation constants in water (DC)		N/A	Molecule does not have the functionality to require this guideline test
830.7550	Partition coefficient		W	Hydrophilic
830.7840	Water solubility		W	High
830.7950	Vapor pressure		W	Solid decomposes
A = Acceptable; N = unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress ; U = Up-grade (additional information required); W = waivers				

830.1800 (Enforcement analytical method): (MRID Nos. 486073-02 & 486073-03)

The enforcement analytical method to determine the active ingredient content in Glufosinate-Ammonium Technical is HPLC/UV. The method is described as follows:

Appendix 1 Analytical Method No. AN091208A-A (Active Ingredient Assay)

ASSAY: Active Ingredient	METHOD NO.: AN091208A-A
MATRIX: Glufosinate Ammonium TGAI	ISSUED: 24 March 2011
	APPROVAL: W Bruce Craig

I. SUMMARY

Glufosinate Ammonium TGAI samples (*ca* 500 mg) are assayed for active ingredient content by HPLC with u.v. detection at 205 nm, following dissolution in mobile phase (100 mL).

II. REAGENTS

1. Glufosinate Ammonium TGAI
2. Glufosinate Ammonium, certified analytical standard
3. Potassium Phosphate, monobasic, AR Grade or equivalent
4. Water, HPLC Grade

III. APPARATUS

1. HPLC: ThermoFinnigan Surveyor
2. Column: PRP-X100 Anion Exchange, 250 x 4.1 mm, 10 μ m
3. Balance: Mettler AE163, 4/5 Figure Analytical Balance
4. Glassware: General Laboratory
5. Data Handling: ThermoElectron XCalibur 2.0 SR2

IV. EXPERIMENTAL CONDITIONS

The following conditions have been established using a ThermoSurveyor HPLC.

Chromatographic conditions may be changed to obtain satisfactory performance with other instruments provided adequate resolution and sensitivity are achieved.

Instrument: ThermoSurveyor HPLC
Column: PRP-X100 Anion Exchange, 250 x 4.1 mm, 10 μ m
Mobile Phase: Potassium Phosphate monobasic (KH₂PO₄)
60 mM in Water
Injection Volume: 10 μ L
Flow Rate: 1.5 mL/min
Temperature: 45° C
Detection: u.v. at 205 nm
Run Time: 10 min
Retention Times: Glufosinate Ammonium at *ca* 2.8 min
Data Handling: ThermoElectron Xcalibur 2.0 SR2

V. PREPARATION OF STANDARD SOLUTIONS

Routine Analysis:

Accurately weigh Glufosinate Ammonium analytical standard (ca 500 mg) into a 100 mL volumetric flask, add exactly 100 mL of mobile phase and shake to dissolve.

Linearity of Response Validation:

A series of Glufosinate Ammonium solutions will be prepared by accurately weighing Glufosinate Ammonium TGA1 (ca 250, 350, 450, 550, 650 and 750 mg) into each of 6, 100 mL volumetric flasks. Add exactly 100 mL of mobile phase and shake to dissolve.

VI. PREPARATION OF QUALITY CONTROL SOLUTIONS

Routine Analysis:

A single sample is prepared for routine use in an identical manner to the analytical standard.

Validation:

Prepare a series of Glufosinate Ammonium solutions by accurately weighing Glufosinate Ammonium analytical standard (ca 400, 400, 500, 500, 600 and 600 mg) into each of 6, 100 mL volumetric flasks. Add exactly 100 mL of mobile phase and shake to dissolve.

VII. PREPARATION OF METHOD PRECISION SAMPLES

Weigh, to the nearest 0.1 mg, sufficient sample to contain 500 mg from a batch of Glufosinate Ammonium TGA1 into a 100 mL volumetric flask. Add exactly 100 mL of mobile phase and shake to dissolve. Prepare 8 samples in this way.

VIII. PREPARATION OF SAMPLES

Weigh in triplicate, to the nearest 0.1 mg, sufficient sample to contain 500 mg Glufosinate Ammonium TGA1 into a 100 mL volumetric flask. Add exactly 100 mL of mobile phase and shake to dissolve.

IX. ANALYSIS OF SAMPLES

Inject 10 μ L of each solution into the chromatograph using the conditions described in Section IV. All standard and sample solutions are injected in duplicate and the peak area for each injection recorded.

A calibration bracketing technique is employed as follows:

Standard, sample, sample, sample, QC, Standard, etc.

X. CALCULATIONS

Integration of all samples is performed using ThermoElectron Xcalibur 2.0 SR2.

Measure the peak areas and calculate the response factors (f_1 and f_2) for the two standards bracketing the 3 individual Glufosinate Ammonium TGA1 samples and the QC recovery sample.

$$f = \frac{Hs}{S}$$

where: Hs = Mean area of Glufosinate Ammonium in the calibration solution.
 S = mass of Glufosinate Ammonium in the calibration solution (mg).

The two response factors (f1 and f2) should be within 2.0% otherwise repeat the assay of the complete group (Standard, Sample 1, Sample 2, Sample 3, QC, Standard)

Calculation: Active content (% w/w) = $\frac{Hw}{f \times w} \times 100$

where: Hw = area of Glufosinate Ammonium in the sample solution.
 f = mean response factor (from f1 and f2).
 w = mass of sample taken (mg).

Assess the system suitability parameters of column efficiency, tailing factor and resolution ratio on a typical sample in accordance with USP, 28th revision, 2005, or equivalent.

The registrant described the validation of the method as follows:

10.1 Validation of Active Ingredient Assay (Analytical Method No. AN091208A-A)

10.1.1 System Suitability (According to USP, 28th Revision 2005)

System suitability was assessed on an Glufosinate Ammonium analytical standard sample (Batch No. EPP/IMD/001/qNMR, 491.9 mg, certified purity of 99.47% w/w).

Column Efficiency (base) = 1412 (Glufosinate Ammonium)
 Tailing Factor = 2.13 (Glufosinate Ammonium)

The active ingredient assay method was found to be specific and sensitive for the purposes of the assay with no interfering peaks noted.

10.1.2 Determination of Linearity of Response

A plot of peak area ratio of Glufosinate Ammonium to internal standard vs. mass of Glufosinate Ammonium in the samples demonstrated excellent linearity, indicated by a correlation coefficient of 0.9999.

Table 1 Linearity of Response: Active Ingredient Assay (Analytical Method No. AN091208A-A)

Concentration Glufosinate Ammonium TGA1 (mg/mL)	Nominal Concentration (% w/w)	Determined Peak Areas		Mean Determined Peak Area	Correlation Coefficient
2.57	51.4	1939705	1952055	1945880	0.9999
3.45	69.0	2597875	2619599	2608737	
4.53	90.6	3370088	3415924	3393006	
5.57	111.4	4143151	4180960	4122056	
6.66	133.2	4907358	4934089	4920724	
7.56	151.2	5488418	5528194	5508306	

10.1.3 Determination of System Precision

The coefficient of variation of 0.3% indicated good system precision.

Table 2 System Precision: Active Ingredient Assay (Analytical Method No. AN091208A-A)

Mass of Glufosinate Ammonium (mg)	Nominal Concentration (% w/w)	Determined Peak Area	Mean Determined Peak Area	Coefficient of Variation (%)
491.9	98.4	3756115	3743069.7	0.3
		3740897		
		3756868		
		3740760		
		3731892		
		3755462		
		3752719		
		3742882		
		3715415		
		3737777		

$$\text{Horwitz Value (\%RSDr)} = 2^{(1-0.5 \log C)} \times 0.67$$

$$= 1.34$$

System Precision < Proposed upper acceptable RSDr limit for 100%

Where C = concentration, C=1 at 100% w/w

10.1.4 Determination of Method Precision

The coefficient of variation of 0.6% indicated good precision for the method.

Table 3 Method Precision: Active Ingredient Assay (Analytical Method No. AN091208A-A)

Mass of Glufosinate Ammonium TGA1	Determined Mass (mg)		Mean Determined Mass (mg)	Mean Determined Concentration (% w/w)	Overall Mean Determined Concentration (% w/w)	Coefficient of Variation (%)
	Replicate 1	Replicate 2				
501.6	495.1	496.3	495.7	98.9	98.2	0.6
511.5	493.0	505.0	499.0	97.6		
492.3	484.2	488.5	486.4	98.8		
492.5	476.1	483.9	480.0	97.5		
505.7	499.6	499.5	499.6	98.8		
545.4	530.3	536.3	533.3	97.8		
502.6	498.1	482.4	490.3	97.6		
508.2	499.7	499.4	499.6	98.3		

$$\text{Horwitz Value (\%RSDr)} = 2^{(1-0.5 \log C)} \times 0.67$$

$$= 1.34$$

System Precision < Proposed upper acceptable RSDr limit for 100%

Where C = concentration, C=1 at 100% w/w

10.1.5 Determination of Assay Accuracy and Precision

The overall assay accuracy (n=6) of 100.0% with a corresponding precision of 0.6% was obtained for Analytical Method No. AN091208A-A, indicating an acceptable method of analysis for Glufosinate Ammonium.

Manufacturing process information may be entitled to confidential treatment

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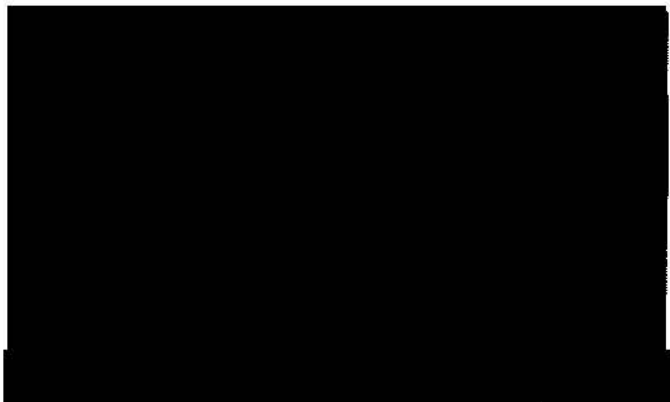
Table 4 Assay Accuracy and Precision: Active Ingredient Assay (Analytical Method No. AN091208A-A)

Mass of Glufosinate Ammonium (mg)	Nominal Concentration (% w/w)	Determined Mass (mg)		Mean Determined Mass (mg)	Mean Recovery (%)	Overall Mean Recovery (%)	Coefficient of Variation (%)
		Replicate 1	Replicate 2				
394.1	ca 80	398.1	395.3	396.7	100.7	100.0	0.6
415.2	ca 80	411.7	418.5	415.1	99.9		
502.0	ca 100	499.2	503.8	501.5	99.9		
507.6	ca 100	510.1	511.7	510.9	100.7		
609.5	ca 120	601.2	607.9	604.6	99.2		
610.8	ca 120	611.8	603.7	607.8	99.5		

Identification of the active ingredient was confirmed by mass spectrometry and infrared spectrophotometry.

830.1600 (Description of materials used to produce the product): (MRID No. 483076-01)

The registrant described the materials used to produce the product (listed on the bottom line) as follows:



MSDSs were provided for the materials.

Product ingredient source information may be entitled to confidential treatment

Manufacturing process information may be entitled to confidential treatment

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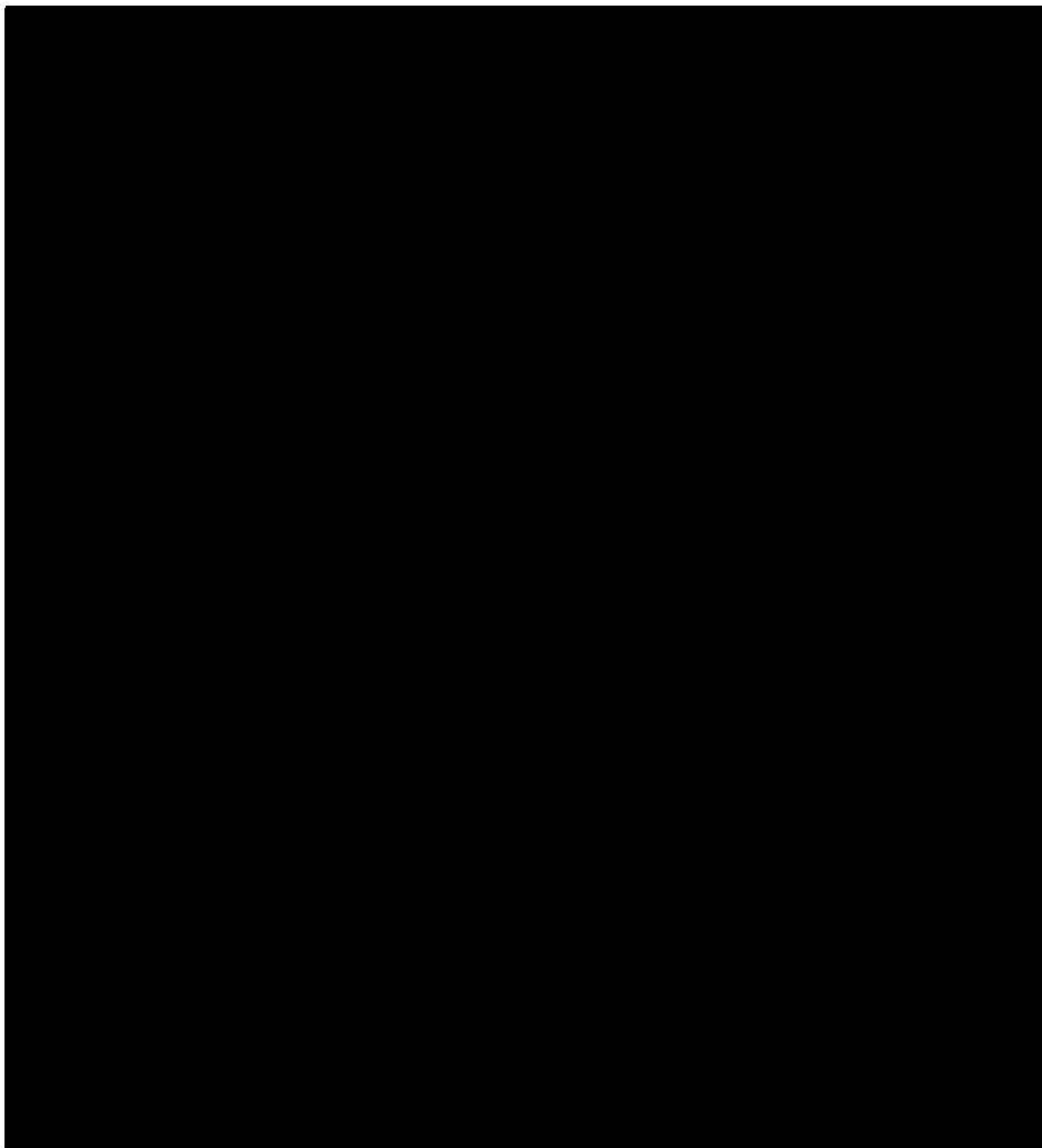
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830.1620 (Description of production process): (MRID No. 486073-01)

Glufosinate-Ammonium Technical will be manufactured by [REDACTED]

[REDACTED] The registrant described the production process as follows:

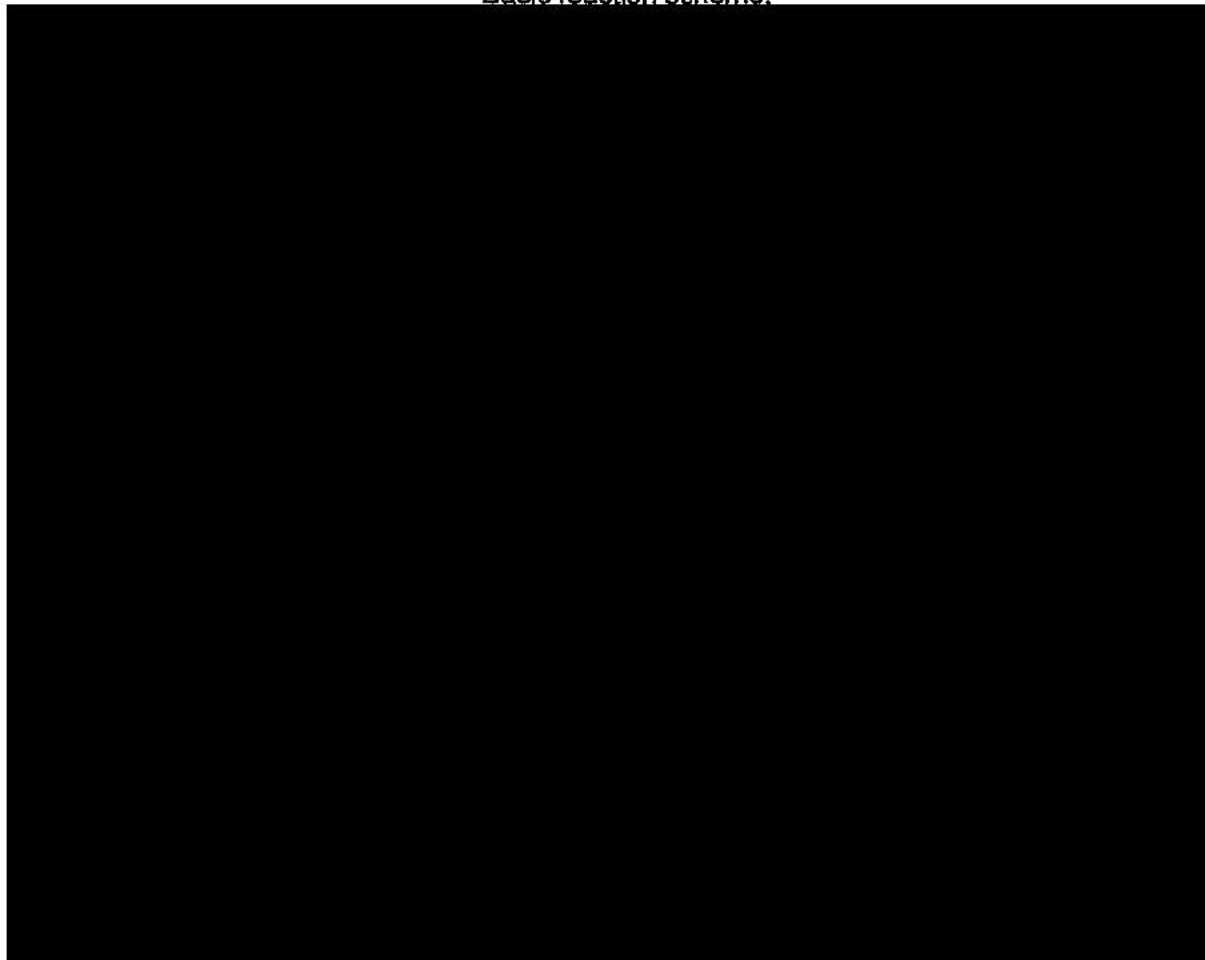
Manufacturing Process



Manufacturing process information may be entitled to confidential treatment

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Basic reaction scheme:

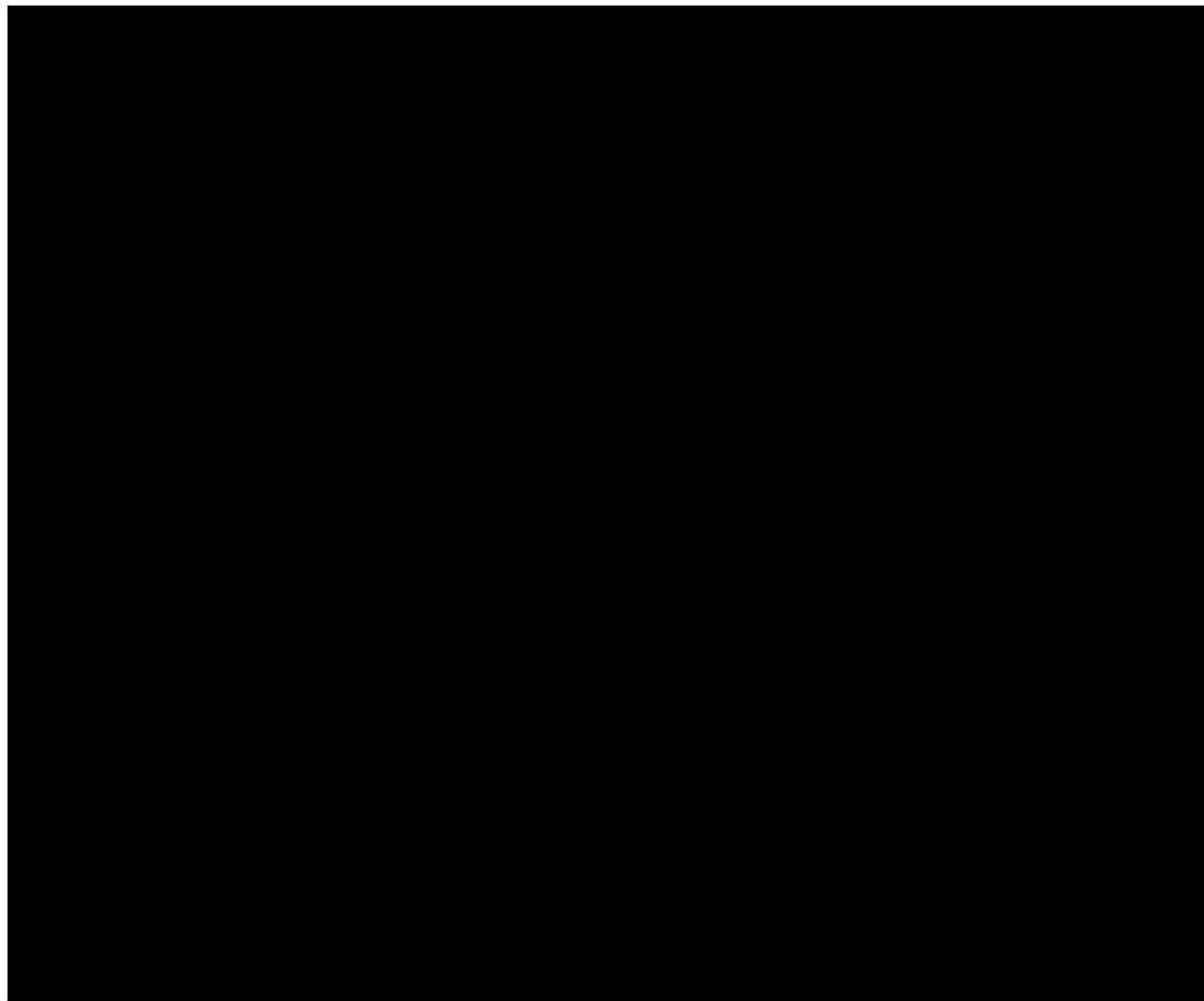


Manufacturing process information may be entitled to confidential treatment

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830.1670 (Discussion on the formation of impurities); (MRID No. 486073-01)

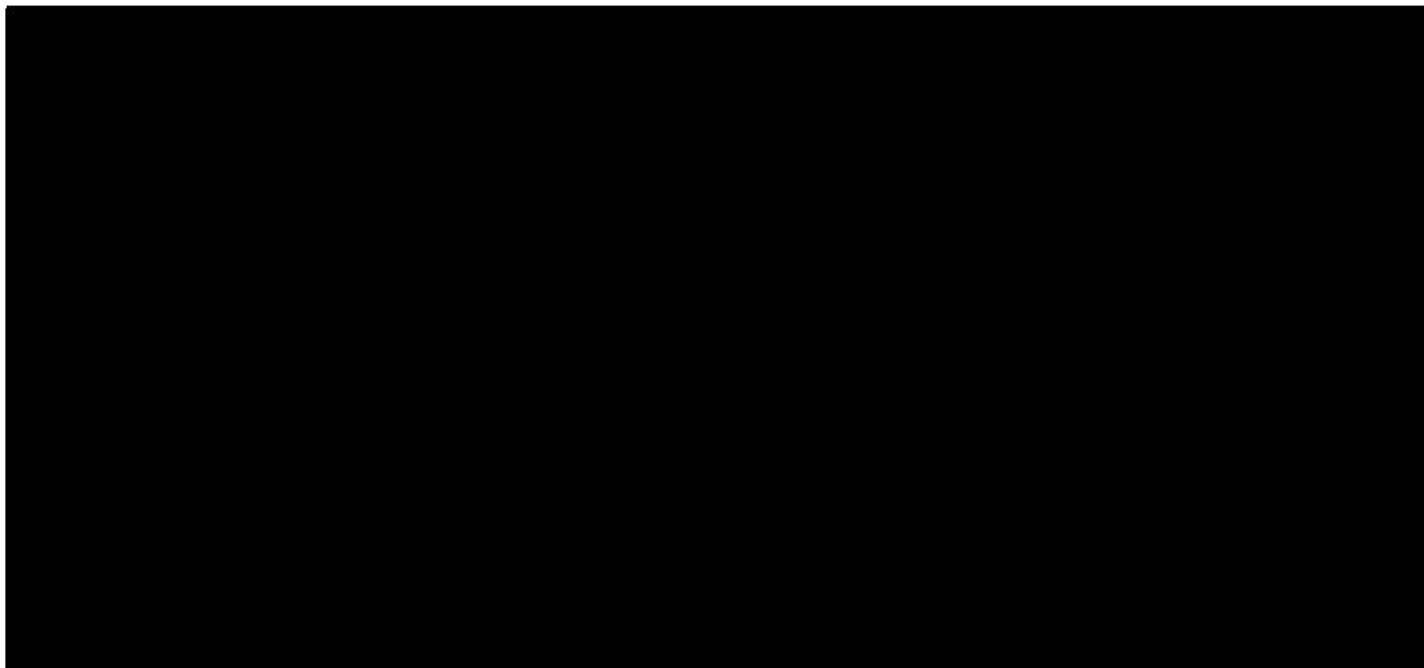
The registrant described the formation of impurities as follows:



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830.1700 (Preliminary analysis): (MRID No. 486073-02)

Results of the preliminary analysis for the active ingredient and impurities in Glufosinate-Ammonium Technical were as follows:



830.1750 (Certified limits): (MRID No. 486073-01)

The certified limits for Glufosinate-Ammonium Technical are provided on the CSF (dated 9/10/2011). The lower certified limit for the active ingredient is within the OCCSP 830.1750 recommended range; the upper certified limit is 100%. The certified limits for the impurities provided in the CSF do not concur with those given in the CSF but the registrant gave an acceptable explanation of how the limits have been calculated for the impurities.